IN THE CLAIMS

Please amend the claims as follows:

--1. (Currently Amended) A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):

B8

$$Y_3$$
 R_1
 R_2
 R_4
 R_6
 X_1
 X_2
 R_5
 X_1
 X_2

wherein Q is H or COC₁₋₈ alkyl;

 R_1 is $C_{1.8}$ alkyl, or one of the following structures:

$$-C$$
 H_2
 Y_2 , C
 H_2
 Y_1

$$\begin{array}{c|c} & & & \\ \hline & & \\ & & \\ & & \\ \end{array} \begin{array}{c} \\ \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \\ \\ \\ \end{array} \begin{array}{c} \\\\ \\ \\ \\ \\ \\ \end{array} \begin{array}{c} \\\\ \\ \\ \\ \\ \\ \end{array} \begin{array}{c} \\\\ \\\\ \\ \\ \\ \end{array} \begin{array}{c} \\\\ \\\\ \\\\ \\ \\ \end{array} \begin{array}{c} \\\\\\ \\\\ \\\\ \end{array} \begin{array}{c}$$

 $Y_{1} \text{ is H, OH, Br, Cl, F, CN, CF}_{3}, NO_{2}, N_{3}, OR_{8}, CO_{2}R_{9}, C_{1.6} \text{ alkyl, NR}_{10}R_{11}, NHCOR_{12}, \\ NHCO_{2}R_{12}, CONR_{13}R_{14}, \underline{or} \ CH_{2}(CH_{2})_{n}Y_{2};$

 Y_2 is H, CF₃, CO₂R₉, C₁₋₆alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, or COCH₂R₉;

 Y_3 is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, or CH₂(CH₂)_nY₂;

 R_2 is H, $C_{1.8}$ alkyl, $C_{3.8}$ alkenyl, $C_{3.8}$ alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

 R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 .

wherein R₂ and R₃ may be bonded together to form a C₂₋₈ alkyl group;

 R_4 is hydrogen, $C_{1.8}$ alkyl, $CO_2C_{1.8}$ alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 or $CO_2C_{1.8}$ alkyl;

Z is N, O or S; where Z is O or S, there is no R,

 R_5 is H_5 C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

R₆ is a group selected from the group consisting of structures (a)-(bbb):

$$(H_{2}C)_{n}$$

$$N$$

$$R_{7}$$

$$R_{7}$$

$$R_{7}$$

$$R_{7}$$

$$R_{7}$$

$$R_{7}$$

$$R_{7}$$

$$R_{7}$$

$$R_{7}$$

$$R_{10}R_{11}$$

$$R_{10}$$

$$R_{11}$$

$$R_{10}$$

$$R_{11}$$

$$R_{11}$$

$$R_{12}$$

$$R_{13}$$

$$R_{14}$$

$$R_{15}$$

$$R_{$$

B8

$$(H_2C)_n$$

$$(H_2C)_n$$

$$R_7$$

$$(d)$$

$$(H_2C)_n$$

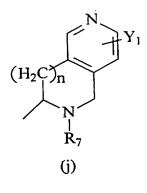
$$R_7$$

$$(e)$$

$$(H_2C)_n$$

$$R_7$$

$$(f)$$



$$(CH_2)_n$$

$$R_7$$

$$(k)$$

$$(H_2C)_n$$

$$R_7$$

$$(I)$$

B&

$$(m) \begin{picture}(20,10) \put(0,0){\line(1,0){10}} \pu$$

$$(H_2C)_n$$
 N
 R_7
 (n)

$$(0)$$

$$Y_1$$

$$N$$

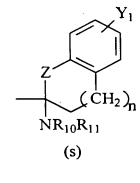
$$(CH_2)_n$$

$$R_7$$

$$R_7$$
 N
 R_7
 (p)

$$N$$
 N
 R_7
 (q)

$$Y_1$$



$$\begin{array}{c} Y_1 \\ \\ X_{10}R_{11} \\ \text{(t)} \end{array}$$

$$(H_2C)_n$$
 $NR_{10}R_{11}$
 (u)

$$(H_2C)_n$$

$$N$$

$$R_7$$

$$(v)$$

$$(H_2C)_n$$

$$X$$

$$Y_1$$

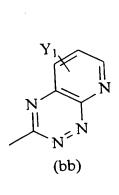
$$X$$

$$Y_1$$

$$X$$

$$Y_1$$

$$\begin{array}{c|c}
Y_1 \\
N \\
\downarrow \\
N \\
\downarrow \\
N \\
\end{array}$$
(y)



$$Y_1$$
 $(CH_2)_n$
 R_7
 (dd)

$$\begin{array}{c} Y_1 \\ \\ \\ \\ \\ NR_{10}R_{11} \\ \text{(ee)} \end{array}$$

$$(H_2C)_n$$
 $NR_{10}R_{11}$
(ff)

$$Y_1 \xrightarrow{H} N$$

$$(CH_2)_n$$

$$R_7$$

$$(gg)$$

$$(H_2C)_n$$
 $NR_{10}R_{11}$
 (hh)

$$Y_1$$
 NH
$$(CH_2)_n$$

$$R_7$$
(ii)

$$(H_2C)_n$$
 $NR_{10}R_{11}$
 (jj)

 $\begin{cases} & & & \\$

$$(H_2C)_n$$

$$NR_{10}R_{11}$$
(II)

$$Y_{1} \nearrow N$$

$$(CH_{2})_{n}$$

$$R_{7}$$

$$(00)$$

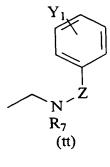
(mm)
$$Y_1$$

$$N_{10}R_{11}$$
(pp)

(CH₂)_n N R₇

$$(CH_2)_n$$
 (qq)

$$\begin{array}{c}
Y_1 \\
Z \\
NR_{10}R_{11} \\
\text{(ss)}
\end{array}$$



$$\begin{array}{c|c}
Y_1 & N \\
 & Z \\
 & R_7 \\
 & (vv)
\end{array}$$

$$Y_{1}$$

$$N$$

$$X_{1}$$

$$X_{1}$$

$$X_{1}$$

$$X_{2}$$

$$X_{3}$$

$$X_{4}$$

$$X_{7}$$

$$X_{7}$$

$$X_{8}$$

$$X_{7}$$

$$X_{8}$$

$$X_{1}$$

$$X_{1}$$

$$X_{2}$$

$$X_{3}$$

$$X_{4}$$

$$X_{5}$$

$$X_{7}$$

$$Y_{1}$$

$$Y_{1}$$

$$Y_{1}$$

$$Y_{2}$$

$$Y_{3}$$

$$Y_{4}$$

$$Y_{2}$$

$$Y_{3}$$

$$Y_{4}$$

$$Y_{5}$$

$$Y_{6}$$

$$Y_{7}$$

$$Y_{8}$$

$$Y_{7}$$

$$Y_{8}$$

$$\begin{array}{c}
Y_1 \\
N \\
NR_{10}R_{11} \\
(xx)
\end{array}$$

$$\begin{array}{c|c}
Y_1 \\
N \\
NR_{10}R_{11} \\
(yy)
\end{array}$$

$$\begin{array}{c} Y_1 \\ N \\ NR_{10}R_{11} \\ (ZZ) \end{array}$$

$$(H_2C)_n$$

$$NR_{10}R_{11}$$
(aaa)

$$R_{11}R_{10}N$$
 $(CH_2)_n$
 (bbb)

```
X_1 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;
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 X_2 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

or X_1 and X_2 together form =0, =S, =NH;

 R_7 is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

 R_8 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$.

 R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

 R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

 R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2;$

 R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_{2;}$

 R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_{2:}$ and

 R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$

2. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z, n, X_1 , X_2 , and R_7 - R_{17} are as indicated above in Claim 1;

Y₃ is H;

 R_2 and R_3 are each, independently, H, $C_{1.8}$ alkyl, $C_{3.8}$ alkenyl, $C_{3.8}$ alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

 R_6 is a group having a formula selected from the group consisting of structures (a)-(cc):

and pharmaceutically acceptable salts thereof.

3. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Y_2 , R_4 , R_5 , Z, n, X_1 , X_2 and R_8 - R_{15} are as indicated above in Claim 1;

R₁ is C₁₋₈ alkyl, or one of the following structures:

$$-\left(\begin{array}{c} C \\ H_2 \\ \end{array}\right) Y_2 , -\left(\begin{array}{c} C \\ H_2 \\ \end{array}\right) Y_1$$

 Y_3 is H;

 R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R₆ is a formula selected from the structures (a)-(r); and

 R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

4. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{15} are as noted above in Claim 1;

0 d

 R_1 is C_{1-8} alkyl;

 Y_2 is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, or COCH₂R₉;

 Y_3 is H;

 R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

 R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, aryl or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R₅ is H, C₁₋₈ alkyl, or CH₂CO₂C₁₋₈ alkyl;

R₆ is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

 R_7 is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

5. (Currently Amended) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{14} are as indicated above in Claim 1;

R₁ is methyl,

 $Y_2 \text{ is } H, CF_3, CO_2R_9, C_{1-6} \text{ alkyl}, NR_{10}R_{11}, NHCOR_{12}, NHCO_2R_{12}, CONR_{13}R_{14}, \\ CH_2OH, CH_2OR_8, \underline{or} COCH_2R_9;$

Y₃ is H;

 R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa; R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R, is H;

 R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

 R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

- 6. (Original) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.
- 7. (Currently Amended) A kappa opioid receptor antagonist compound represented by the formula (I):

$$Y_3$$
 R_1
 R_2
 R_4
 R_6
 X_1
 X_2
 R_5
 X_1
 X_2

wherein Q is H or COC₁₋₈ alkyl;

 R_1 is C_{1-8} alkyl, or one of the following structures:

$$\begin{array}{c}
C \\
H_2 \\
N
\end{array}$$

$$\begin{array}{c}
C \\
H_2 \\
N
\end{array}$$

$$\begin{array}{c}
N \\
N \\
N \\
N
\end{array}$$

$$\begin{array}{c}
N \\
N \\
N \\
N
\end{array}$$

$$\begin{array}{c}
N \\
N \\
N \\
N \\
N
\end{array}$$

 Y_1 is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, or CH₂(CH₂)_nY₂;

 Y_2 is H, CF₃, CO₂R₉, C₁₋₆alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, or COCH₂R₉;

 Y_3 is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, or CH₂(CH₂)_nY₂;

 R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

 R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 .

wherein R₂ and R₃ may be bonded together to form a C₂₋₈ alkyl group;

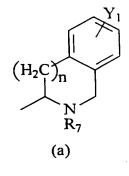
 R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S there is no R₅

 R_5 is H, $C_{1.8}$ alkyl, $C_{3.8}$ alkenyl, $C_{3.8}$ alkynyl, $CH_2CO_2C_{1.8}$ alkyl, $CO_2C_{1.8}$ alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

 R_6 is a group selected from the group consisting of structures (a)-(bbb):



$$Y_1$$
 $(CH_2)_n$
 (B)

$$(CH_2)_{n}$$

$$(CH_2)_{n}$$

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$$(H_2C)_n$$
 R_7
 (d)

$$(e)$$

$$Y_1 \qquad H \qquad H \qquad N$$

$$(CH_2)_n \qquad (CH_2)_n$$

$$(H_2C)_n$$
 N
 R_7
 (f)

$$Y_1$$
 NH
$$(CH_2)_n$$

$$R_7$$

$$(g)$$

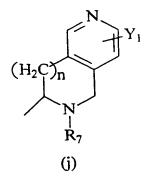
$$(H_2C)_n$$

$$\begin{pmatrix} N & Y_1 \\ N & \\ N & \\ R_7 \\ (h) & \end{pmatrix}$$

$$(i)$$

$$Y_1$$

$$CH_2)_n$$



$$(H_2C)_n$$

$$R_7$$

$$(I)$$

B&

$$Y_{1}$$

$$N$$

$$(CH_{2})_{n}$$

$$R_{7}$$

$$(m)$$

$$(H_2C)_n$$
 N
 R_7
 (n)

$$(0)$$

$$Y_1$$

$$N$$

$$CH_2$$

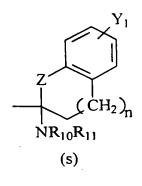
$$n$$

$$(0)$$

$$R_7$$
 N
 R_7
 (p)

$$N$$
 N
 R_7
 (q)

$$Y_1$$
 Y_1
 Y_1



$$\begin{array}{c}
Y_1 \\
X_1 \\
X_1 \\
X_2 \\
X_3 \\
X_4 \\
X_5 \\
X_6 \\
X_7 \\
X_7 \\
X_8 \\
X_8 \\
X_8 \\
X_9 \\
X_9$$

$$(H_2C)_n$$
 $NR_{10}R_{11}$
 (u)

 $\mathcal{F}^{\mathcal{E}}$ $(H_2C)_n$ R_7 (Y)

$$(H_2C)_n$$

$$N$$

$$R_7$$

$$Y_1$$

$$R_7$$

$$(w)$$

$$\begin{array}{c|c}
Y_1 & N \\
N & N
\end{array}$$
(z)

$$(H_2C)_n$$
 Y_1
 (cc)

$$Y_1$$

$$(CH_2)_n$$

$$R_7$$

$$(dd)$$

$$\begin{array}{c} Y_1 \\ \\ \\ \\ \\ NR_{10}R_{11} \\ \\ \text{(ee)} \end{array}$$

$$(H_2C)_n$$

$$NR_{10}R_{11}$$
(ff)

$$\begin{array}{c}
Y_1 & H \\
N & N \\
(CH_2)_n & R_7 \\
(gg)
\end{array}$$

$$(H_2C)_n$$
 $NR_{10}R_{11}$
 (hh)

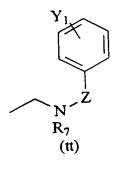
$$Y_1$$
 NH
 $(CH_2)_n$
 R_7
 (ii)

(jj)

 $\left(H_2C\right)_n$ $NR_{10}R_{11}$ N I R₇ (mm) **(ll)** (kk) $\left(H_2C\right)_n$ $\left(H_2C\right)_n$ $NR_{10}R_{11}$ $NR_{10}R_{11}$ (pp) (00) (nn) (CH₂)_n N R₇ $NR_{10}R_{11}$ $NR_{10}R_{11}$ (ss)

(rr)

(qq)



$$\begin{array}{c|c}
Y_1 & N \\
 & X \\
N & Z \\
R_7 & (vv)
\end{array}$$

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$$\begin{array}{c|c}
Y_1 & N \\
NR_{10}R_{11} \\
(xx)
\end{array}$$

$$\begin{array}{c}
Y_1 \\
N \\
NR_{10}R_{11} \\
(yy)
\end{array}$$

$$\begin{array}{c|c}
Y_1 \\
N \\
NR_{10}R_{11}
\end{array}$$
(zz)

$$(H_2C)_n$$

$$NR_{10}R_{11}$$
(aaa)

$$R_{11}R_{10}N$$
 $(CH_2)_n$
 (bbb)

nd

 X_1 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

 X_2 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, or C_{3-8} alkynyl;

or X_1 and X_2 together form =0, =S, or =NH;

 R_7 is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$.

 R_8 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$.

 R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

 R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$,

 R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

 R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_{2;}$

 R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$; and

 R_{17} is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$

and pharmaceutically acceptable salts thereof.

8. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein R₁, R₄, R₅, Y₁, Y₂, Z, n, X₁, X₂, and R₇-R₁₇ are as indicated above in Claim 7;

Y₃ is H;

 R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

 R_6 is a group having a formula selected from the group consisting of structures (a)-(cc).

9. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein Y₁, Y₂, R₄, R₅, Z, n, X₁, X₂ and R₈-R₁₅ are as indicated above in Claim 7;

 R_1 is C_{1-8} alkyl, or one of the following structures:

$$-C$$
 H_2
 Y_2
 Y_1

 Y_3 is H;

 R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

 R_6 is a formula selected from the structures (a)-(r) shown above; and

 R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

10. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{15} are as noted above in Claim 7;

R₁ is C₁₋₈ alkyl;

 $Y_2 \text{ is H, CF}_3, CO_2R_9, C_{1-6} \text{ alkyl, NR}_{10}R_{11}, \text{NHCOR}_{12}, \text{NHCO}_2R_{12}, \text{CONR}_{13}R_{14}, \text{CH}_2\text{OH,}$ $\text{CH}_2\text{OR}_8, \text{ or COCH}_2R_9;$

 Y_3 is H;

R₂ and R₃ are each, independently, H or methyl, wherein R₂ and R₃ cannot both be H at the same time;

 R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, aryl or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R₅ is H, C₁₋₈ alkyl, CH₂CO₂C₁₋₈ alkyl;

R₆ is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

 R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

11. (Currently Amended) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{14} are as indicated above in Claim 7;

 R_1 is methyl,

 Y_2 is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, or COCH₂R₉;

 Y_3 is H;

 R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa; R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R₅ is H;

 R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

 R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

12. (Original) The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae 14-21 of Fig. 1.

13. (Currently Amended) A pharmaceutical composition comprising:

an effective amount of a kappa opioid receptor antagonist and a physiologically
acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula

(I):

$$Y_3$$
 R_1
 R_2
 R_4
 R_6
 X_1
 X_2
 R_5
 X_1
 X_2

wherein Q is H or COC₁₋₈ alkyl;

 R_1 is C_{1-8} alkyl, or one of the following structures:

$$C \longrightarrow Y_2$$
, $C \longrightarrow Y_1$

$$\begin{array}{c|c} & & & \\ \hline & &$$

 Y_1 is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, or CH₂(CH₂)_nY₂;

 $Y_2 \text{ is H, CF}_3, CO_2R_9, C_{l-6}alkyl, NR_{10}R_{11}, NHCOR_{12}, NHCO_2R_{l2}, CONR_{13}R_{l4}, CH_2OH, \\ CH_2OR_8, \text{ or } COCH_2R_9;$

 Y_3 is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, or CH₂(CH₂)_nY₂;

 R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups Y_1 ;

 R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2 aryl substituted by one or more groups $Y_{1:}$

wherein R₂ and R₃ may be bonded together to form a C₂₋₈ alkyl group;

 R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1 , CH_2 aryl substituted by one or more groups Y_1 , or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S, there is no R₅

 R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2 aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

R₆ is a group selected from the group consisting of structures (a)-(bbb):

$$(H_2C)_n$$

$$N$$

$$R_7$$

$$R_7$$

$$R_7$$

$$(b)$$

$$NR_{10}R_{11}$$

$$(c)$$

$$(H_2C)_n$$
 R_7
 (d)

$$Y_1 \longrightarrow H$$

$$N$$

$$(CH_2)_n$$

$$R_7$$

$$(e)$$

$$(H_2C)_n$$
 N
 R_7
 (f)

$$Y_1$$
 NH NH CH_2 NH R_7 (g)

$$(i)$$

$$Y_1$$

$$CH_2)_n$$

$$R_7$$

$$(H_2C)_n$$

$$N$$

$$R_7$$

$$(j)$$

$$(CH_2)_n$$
 $(R_7)_n$
 (k)

$$(H_2C)_n$$
 N
 R_7
 (1)

$$(H_2C)_n$$

$$N$$

$$R_7$$

$$(n)$$

$$(0)$$

$$Y_1$$

$$N$$

$$N$$

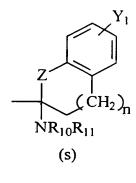
$$(CH_2)_n$$

$$R_7$$

$$R_7$$
 N
 R_7
 (p)

$$N$$
 N
 N
 R_7
 R_7
 R_7

$$Y_1$$
 Y_1
 Y_1



$$X_{10}$$
 X_{10}
 X_{10}
 X_{10}
 X_{10}

$$(H_2C)_n$$
 $NR_{10}R_{11}$
 (u)

$$(H_2C)_n$$
 Y_1
 R_7
 (v)

$$(H_2C)_n$$

$$X$$

$$Y_1$$

$$X$$

$$Y_1$$

$$X$$

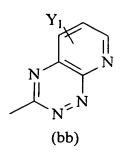
$$Y_1$$

$$X$$

$$Y_1$$

$$\begin{array}{c|c}
Y_1 & N \\
N & N \\
N & N
\end{array}$$
(z)

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$$(H_2C)_n$$
 Y_1
 (cc)

$$\begin{array}{c}
Y_1 \\
& \\
& \\
& \\
N \\
R_7 \\
& \\
& \\
(dd)
\end{array}$$

$$\begin{array}{c} Y_1 \\ \\ \swarrow \\ (CH_2)_n \\ NR_{10}R_{11} \\ \text{(ee)} \end{array}$$

$$(H_2C)_n$$

$$NR_{10}R_{11}$$
(ff)

$$\begin{array}{c}
Y_1 & H \\
N & N \\
(CH_2)_n \\
R_7 \\
(gg)
\end{array}$$

13 8

$$(H_2C)_n$$
 $NR_{10}R_{11}$
 (hh)

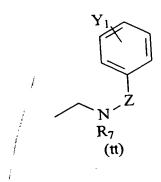
$$Y_1$$
 NH
 $(CH_2)_n$
 R_7
 (ii)

$$(H_2C)_n$$

$$NR_{10}R_{11}$$

$$(jj)$$

$$\begin{array}{c|c} Y_1 \\ & & \\ N \\ & & \\ (CH_2)_n \\ & & \\ NR_{10}R_{11} \\ & & \\ R_7 \\ & & \\ (qq) \end{array}$$



 β N R_7 (ww)

$$\begin{array}{c|c}
Y_1 & N \\
NR_{10}R_{11} \\
(xx)
\end{array}$$

$$\begin{array}{c|c}
Y_1 & & \\
N & N \\
NR_{10}R_{11} & \\
(zz) & & \end{array}$$

$$(H_2C)_n$$

$$NR_{10}R_{11}$$
(aaa)

$$R_{11}R_{10}N$$
 $(CH_2)_n$
 (bbb)

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X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

X₂ is hydrogen, C₁₋₈alkyl, C₃₋₈alkenyl, or C₃₋₈alkynyl;

or X_1 and X_2 , together form =0, =S, =NH;

 R_7 is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

 R_8 is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$.

 R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$;

 R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{12} is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_{2i}$

 R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$.

 R_{16} is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_{2:}$ and

 R_{17} is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , or $CH_2(CH_2)_nY_2$

or a pharmaceutically acceptable salt thereof.

14. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1 , R_4 , R_5 , Y_1 , Y_2 , Z_5 , Z_1 , Z_2 , and Z_3 , and Z_4 , are as indicated above in Claim 13;

 Y_3 is H;

BB

 R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2 aryl substituted by one or more substituents Y_1 ; and

R₆ is a group having a formula selected from the group consisting of structures (a)-(cc).

15. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Y_2 , R_4 , R_5 , Z, n, X_1 , X_2 and R_8 - R_{15} are as indicated above in Claim 13;

R₁ is C₁₋₈ alkyl, or one of the following structures:

 Y_3 is H;

 R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R₆ is a formula selected from the structures (a)-(r) shown above; and

 R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

16. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{15} are as noted above in Claim 13;

 R_1 is C_{1-8} alkyl;

 Y_2 is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, or COCH₂R₉;

 Y_3 is H;

· * * * * * *

 R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

 R_4 is H, C_{1-8} alkyl, CO_2C_{1-8} alkyl, aryl or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

 $\rm R_5$ is H, $\rm C_{1-8}$ alkyl, $\rm CH_2CO_2C_{1-8}$ alkyl;

 R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

 R_7 is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

17. (Currently Amended) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z, n, X_1 , X_2 and R_8 - R_{14} are as indicated above in Claim 13;

R₁ is methyl,

 Y_2 is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, or COCH₂R₉;

 Y_3 is H;

 R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa; R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a

R₅ is H;

configuration of (S);

 R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

 R_7 is H, $C_{1.8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

- 18. (Original) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.
- 19. (Original) The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.
- 20. (Original) The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

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- 21. (Original) The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.
- 22. (Currently Amended) The kappa opioid receptor antagonist according to Claim 7, having the chemical formula:

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- 23. (New) The method of binding a kappa opioid receptor in a subject in need thereof, as claimed in claim 1, wherein R_1 is C_{1-8} alkyl; $(CH_2)_n$ - Y_2 ; $(CH_2)_n$ -phenyl- Y_1 ; or $(CH_2)_n$ -pyridyl- Y_1 , and R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1 - Y_3 , R_2 - R_5 , Z, R_1 , X_2 , and R_7 - R_{17} are as in Claim 1.
- 24. (New) The kappa opioid receptor antagonist compound as claimed in claim 7, wherein R_1 is C_{1-8} alkyl; $(CH_2)_n$ - Y_2 ; $(CH_2)_n$ -phenyl- Y_1 ; or $(CH_2)_n$ -pyridyl- Y_1 , and R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1 - Y_3 , R_2 - R_5 , Z, n, X_1 , X_2 , and R_7 - R_{17} are as in Claim 7.
- 25. (New) The pharmaceutical composition as claimed in claim 13, wherein R_1 is C_1 . 8alkyl; $(CH_2)_n$ - Y_2 ; $(CH_2)_n$ -phenyl- Y_1 ; or $(CH_2)_n$ -pyridyl- Y_1 , and R_6 is a group selected from

the group consisting of structures (a)-(w) and (cc)-(bbb), and wherein Q, Y_1 - Y_3 , R_2 - R_5 , Z, n, X_1 , X_2 , and R_7 - R_{17} are as in Claim 13.--